

Prostatitis due to penicillinase-producing *Neisseria gonorrhoeae*

Case reports

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SUMMARY Complicated infections caused by penicillinase-producing *Neisseria gonorrhoeae* (PPNG) are uncommon. Of two patients with prostatitis due to PPNG, one was cured by cefoxitin followed by co-trimoxazole, the other by co-trimoxazole alone. The potential of co-trimoxazole in the treatment of PPNG-prostatitis looks promising.

Introduction

Since their first isolation in the United States¹ and the United Kingdom,² penicillinase-producing *Neisseria gonorrhoeae* (PPNG) strains have been isolated in many countries. In The Netherlands the number of cases of gonorrhoea caused by PPNG has been constantly increasing (18% of all cases in December 1980³). In the treatment of uncomplicated infections due to PPNG, spectinomycin and the new cephalosporins, cefuroxime and cefoxitin, are the drugs of choice. Until now, no particular treatment schedule for complicated forms of gonorrhoea caused by β -lactamase-producing strains has met with general approval. Recently we saw two men with complicated PPNG infections; one had prostatitis and the other prostatitis and epididymo-orchitis. Because of the poor penetration of spectinomycin into prostatic tissue one patient was treated with cefoxitin followed by co-trimoxazole and the other with co-trimoxazole alone.

Case reports

CASE 1

A 26-year-old man was admitted to the Department of Dermatology, University Hospital, Utrecht, after having been treated with doxycycline for a venereal infection by his general practitioner five weeks previously. Shortly afterwards, after a new sexual contact, he developed swelling of the left testis, low

abdominal pain, low back pain, painful micturition, and shivering. He had a swelling of the left testis and epididymis. The left groin was painful with a few palpable inguinal lymph nodes. The prostate was enlarged and painful. Cultures of the urine for eubacteria gave negative results, but a β -lactamase-producing strain of *Neisseria gonorrhoeae* (PPNG) was isolated from the urethra. The minimum inhibitory concentrations (MICs) for the strain were: penicillin, >16 μ g/ml; tetracycline, 1 μ g/ml; sulphonamides, 4 μ g/ml; trimethoprim, 6.4 μ g/ml; trimethoprim and sulphamethoxazole (co-trimoxazole), 4 μ g/ml and 0.2 μ g/ml respectively; and cefoxitin, 0.12 μ g/ml.

His haemoglobin concentration was 14.2 g/dl, the haematocrit 43%, white cell count $6.2 \times 10^9/l$, with 73% neutrophils, 14% lymphocytes, 4% monocytes, 9% eosinophils, and 0% basophils. Liver and renal function test results were within normal limits. Initially, the patient was treated with 1.8 g benzylpenicillin intravenously four times a day for five days. Once the antibiotic resistance pattern was known, treatment was changed to cefoxitin in a 1-g intravenous dose six times a day. After five days of treatment with cefoxitin only the epididymis was still enlarged. Intravenous treatment was discontinued and the patient treated with co-trimoxazole 1.44 g by mouth twice daily for three weeks. Four days after the beginning of treatment with co-trimoxazole *N. gonorrhoeae* could not be isolated from the urethra. After two weeks the patient was free of symptoms and was discharged from hospital. Five months later he reattended the outpatient clinic; on this occasion he had urethritis due to a strain of *N. gonorrhoeae* which was sensitive to penicillin.

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CASE 2

A 21-year-old man was admitted for investigation of haematuria and strangury. One week previously he had complained of low back pain, pain in the perineum, and difficulty in urinating. His family practitioner had prescribed nitrofurantoin. Since 1979 he was known to have diabetes mellitus. In September 1980 he completed a year's course of treatment for pulmonary tuberculosis.

On admission the only clinical abnormality was an enlarged painful prostate gland. The white cell count was $15 \times 10^9/l$ with a normal differential count. The erythrocyte sedimentation rate was 30 mm/first hour. Although the urine contained many polymorphonuclear leucocytes no organisms were isolated on culture. A β -lactamase-producing strain of *N gonorrhoeae* was isolated, however, from urine passed immediately after prostatic massage. The MICs were: penicillin, $>16 \mu\text{g/ml}$; tetracycline, $1 \mu\text{g/ml}$; erythromycin, $<0.12 \mu\text{g/ml}$; spectinomycin, $8 \mu\text{g/ml}$; sulphonamides, $4 \mu\text{g/ml}$; trimethoprim, $6.4 \mu\text{g/ml}$; trimethoprim and sulphamethoxazole (co-trimoxazole) $4 \mu\text{g/ml}$ and $0.2 \mu\text{g/ml}$ respectively; and cefoxitin, $<0.12 \mu\text{g/ml}$. Intravenous pyelography showed a horseshoe kidney. The patient was treated with co-trimoxazole 1.44 g by mouth twice daily for three weeks. His condition improved rapidly and *N gonorrhoeae* was not isolated from the urethra on the tenth day of treatment nor one week after completion of treatment.

Discussion

Before the isolation of PPNG in 1976 a gradual increase in the resistance of gonococci to penicillin had been reported in several countries; this necessitated the use of increasing doses of penicillin for effective treatment. Strains isolated from complicated forms of gonorrhoea, however, were found to be notably more susceptible to penicillin G,⁴ so that the relative resistance to penicillin did not constitute a problem in patients with complicated infections. Little is known about the virulence of PPNG; only a few cases of complicated infection have been reported.⁵⁻⁷ According to a recent review of infections due to PPNG in the United States in 1976-80⁸ the frequency of salpingitis complicating cervical gonorrhoea in women with infections due to PPNG was similar to that reported for women with non-PPNG infections. With the constant increasing rate of infections due to PPNG, however, an increased incidence of complications of gonococcal infections due to PPNG can be expected. Of these, prostatitis is a particular problem because of the poor penetration of antibiotics into prostatic tissue and fluid. Spectinomycin, the drug of choice for uncomplicated

PPNG infections is an aminocyclitol and unlikely to reach therapeutic concentrations in the prostate.⁹ The newer cephalosporins, cefuroxime, cefoxitin, and cefotaxime, have been used successfully to treat uncomplicated gonorrhoea,^{10 11} but, in general, concentrations of cephalosporin in prostatic tissue are low.⁹ These antibiotics are probably not adequate for treating prostatitis due to PPNG. Co-trimoxazole has been suggested as an alternative treatment for gonorrhoea caused by penicillin-sensitive and penicillin-resistant strains.¹²⁻¹⁴ Trimethoprim potentiates the action of sulphamethoxazole against gonococci¹⁵; the concentration in prostatic tissue exceeds the simultaneous plasma concentration.¹⁶ Administration of tablets of the usual combined preparation with a sulphamethoxazole:trimethoprim ratio of 5:1 results in a 20:1 ratio of the agents in the blood. This situation is reversed in the tissues to an extent which depends on the tissue involved. In prostatic tissue¹⁶ this is favourable since the optimum sulphamethoxazole:trimethoprim ratio for *N gonorrhoeae* is lower than that for other organisms and requires more trimethoprim¹⁵; the administration of the usual tablets of the combined preparation should be adequate for the treatment of gonococcal prostatitis.

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